

TOOLS FOR GENETIC STUDIES IN ZEBRAFISH

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Trans-NIH Zebrafish Coordinating Committee

(<http://www.nih.gov/science/models/zebrafish/>)

National Institute of Child Health and Human Development (NICHD)

(<http://www.nichd.nih.gov/>)

National Cancer Institute (NCI)

(<http://www.nci.nih.gov/>)

National Center for Research Resources (NCRR)

(<http://www.ncrr.nih.gov/>)

National Eye Institute (NEI)

(<http://www.nei.nih.gov/>)

National Heart, Lung, and Blood Institute (NHLBI)

(<http://www.nhlbi.nih.gov/index.htm>)

National Human Genome Research Institute (NHGRI)

(<http://www.nhgri.nih.gov/>)

National Institute on Aging (NIA)

(<http://www.nih.gov/nia/>)

National Institute on Alcohol Abuse and Alcoholism (NIAAA)

(<http://www.niaaa.nih.gov/>)

National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)

(<http://www.nih.gov/niams/>)

National Institute on Deafness and Other Communication Disorders (NIDCD)

(<http://www.nidcd.nih.gov/>)

National Institute of Dental and Craniofacial Research (NIDCR)

(<http://www.nidr.nih.gov/>)

National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)

[\(http://www.niddk.nih.gov/\)](http://www.niddk.nih.gov/)

National Institute on Drug Abuse (NIDA)

[\(http://www.nida.nih.gov/\)](http://www.nida.nih.gov/)

National Institute of Environmental Health Sciences (NIEHS)

[\(http://www.niehs.nih.gov/\)](http://www.niehs.nih.gov/)

National Institute of General Medical Sciences (NIGMS)

[\(http://www.nigms.nih.gov/\)](http://www.nigms.nih.gov/)

National Institute of Mental Health (NIMH)

[\(http://www.nimh.nih.gov/\)](http://www.nimh.nih.gov/)

National Institute of Neurological Disorders and Stroke (NINDS)

[\(http://www.ninds.nih.gov/\)](http://www.ninds.nih.gov/)

THIS PA CONTAINS THE FOLLOWING INFORMATION

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PURPOSE OF THIS PA

This Program Announcement (PA) is to encourage investigator-initiated applications for research designed to exploit the power of mutagenesis screening in zebrafish in order to detect and characterize genes, pathways, and phenotypes of interest in development and aging, organ formation, behavior, and disease processes. Applications that propose to advance the technologies associated with such phenotyping also are welcome. A secondary goal of this PA is to ensure that tools developed under this initiative are widely available to the research community. This PA is a continuation of the program initiated by RFA HD-00-004, "Mutagenesis Screens/Phenotyping Tools for Zebrafish" (<http://grants.nih.gov/grants/guide/rfa-files/RFA-HD-00->

[004.html](#)), and incorporates an earlier PA, "Development of Zebrafish Mutagenesis and Screening Tools" (<http://grants.nih.gov/grants/guide/pa-files/PA-01-070.html>). This effort stems from an NIH initiative with participation of the Institutes and Centers listed above, working through the Trans-NIH Zebrafish Coordinating Committee (TZCC; <http://www.nih.gov/science/models/zebrafish/>) under the co-chairmanship of NICHD and NIDDK. Since its formation in 1997, the committee has played an active role as an advocate for the zebrafish as an important model for development and disease research.

RESEARCH OBJECTIVES

Background

The TZCC continues to play an active role as an advocate for the zebrafish model. On May 10-11, 1999 and on April 1-2, 2002, the TZCC sponsored workshops entitled, "Genomic and Genetic Tools for the Zebrafish," at which zebrafish researchers were asked to help prioritize the short- and long-term needs of the community. One result of the workshops was the recommendation that more genetic screens and more tools for carrying out mutagenesis in the zebrafish need to be supported by the NIH. It also became clear that it is critical for non-hypothesis driven, tool development proposals to be reviewed as a group, within a single framework. RFA-HD-00-004, "Mutagenesis Screens/Phenotyping Tools for Zebrafish," addressed this need, in part. The current PA continues NIH efforts to support the development of additional mutants and additional tools for genetic studies in the zebrafish.

As a vertebrate, the zebrafish, *Danio rerio*, is more closely related to humans than are yeast, worms, or flies. It has a number of advantageous features as a model organism for the study of vertebrate development, disease, and biological pathways, which have been validated further by the demonstration that many zebrafish genes show a high degree of structural and functional similarity to their human homologues. The most powerful and unique feature of the zebrafish is that it is a vertebrate model organism with a proven track record of easily executed, large-scale forward mutagenesis screens. Nevertheless, there is a need for more mutants as, for example, few screens have been carried out to identify mutations affecting adult behavior, physiology, or morphology. In addition, there are few tools for targeted gene knockout, conditional gene expression, enhancer trapping, or rapid insertional mutagenesis. The two goals of the PA, identifying additional mutants and developing new genetic tools, are synergistic, as the availability of more efficient tools will make screens easier and the discovery of mutants affecting important processes will stimulate additional research on methods to study those mutants.

Research Scope

The objective of this PA is to continue to broaden the range, power, and utility of screens for new mutants of zebrafish. It will, therefore, support proposals for development of improved or novel methods for mutagenesis screens, as well as proposals for the actual execution of such screens. Methodology developed and data and mutants generated as a result of this PA are expected to be made widely available to the research community. Applicants must include as part of their applications a plan for disseminating these resources (see SPECIAL REQUIREMENTS, below); adequacy of this plan will be considered in making funding decisions for applications responding to this PA (see AWARD CRITERIA, below). Objectives to be addressed in applications submitted in response to this PA include, but are not limited to, the following:

- o Development and/or application of novel methods of mutagenesis (e.g., insertional, site-specific, conditional knockout vectors or systems).

- o Development and/or application of novel screens for mutants. These may be:

Phenotypic screens based on observation of alterations in morphology, physiology, or behavior;

Genetic screens focusing on identifying mutations that affect the structure and function of specific tissue/organ systems;

Screens focusing on identifying novel developmental genes and pathways, including those mediating sensitivity or resistance to environmental teratogens;

Screens to analyze the genetic basis of adult phenotypes including behavior, aging, organ disease, cancer, and responses to environmental toxins, alcohol, and drugs of abuse;

Sensitized screens, using strains carrying a known mutation, in order to identify extragenic suppressors or enhancers of that mutation.

- o Development of systems for rapid mapping or identification of point mutations.

- o Development of technology for gene inactivation and for gene expression manipulation including, but not limited to, morpholino oligonucleotides, new types of antisense technology,

techniques for homologous recombination, techniques for gene trapping, and strategies for directing gene misexpression, or other transgenic methodologies.

Interests of Participating Institutes and Centers

The participating NIH Institutes and Centers have provided a brief outline of their interests as they relate to the goals of this PA. These brief mission statements are intended to indicate the breadth of the biomedical areas of interest in which zebrafish are likely to be a useful model.

NCI: Generation and study of zebrafish models to identify and place genes in functional pathways that affect growth and development; in particular, genes/pathways that, when altered, result in uncontrolled or cancerous growth.

NCRR: The NCRR supports research projects that broaden the utility of the zebrafish model for cross-cutting biomedical research that is not encompassed within a single NIH Institute or Center. Interests include, but are not limited to, development of new methods for mutagenesis and/or phenotypic characterization that would be of use in research on a wide range of diseases or organs, particularly if these methods could be applied to other animal models as well as the zebrafish.

NEI: Fundamental mechanisms underlying all aspects of eye development, function, and disease, including development of the retina and lens, optic nerve axon guidance, and the neural circuitry producing eye movements and oculomotor behaviors.

NHLBI: Cellular and molecular functions of the mutant genes in development as models for human cardiovascular, blood, and pulmonary disorders, and circadian mechanisms regulating rest/activity cycles. Genetic basis of disorders of cardiovascular development and function; developmental aspects of endothelial dysfunction as the basis for systemic and pulmonary vascular disorders; developmental defects in hematopoiesis and relationship to disorders of the hematopoietic system; genetic basis of angiogenesis and vasculogenesis; effect of mutations on subsequent organ development leading to such disorders as arrhythmia, cardiac hypertrophy, dilated cardiomyopathy, heart failure, lung hypoplasia and bronchopulmonary dysplasia; the genetic basis, regulation, and role of biological clock mechanisms in development and circadian behavior.

NHGRI: Proposals for the development of high throughput, widely applicable technologies or methodologies to examine gene function on a genomic scale. This could include initial

development of high throughput or large-scale methods for examining gene expression, development of tools for comprehensive mutational analysis or genome-scale identification of regulatory regions.

NIA: Basic research on the genetic and molecular basis of aging and longevity. Generation and analysis of late-age onset or long-lived mutants that can be used to identify, clone, and characterize genes involved in normal and pathological aging. Cellular and molecular function of genes expressed, for example, in the aging nervous system, cardiovascular, immune, and musculoskeletal systems. Such genes include, but are not limited to, those involved in neurodegenerative disorders, neuroplasticity, cell death, damage and repair of DNA and proteins, and oxidative metabolism, and maintenance of differentiated cell function.

NIAAA: Mechanistic studies of ethanol-induced teratogenesis, behavioral impairments, and organ damage. These studies may include screening methods for alcohol-related phenotypes, gene identification, and functional analyses of these genes.

NIAMS: Mutations that have the potential to illuminate the development and function of the vertebrate musculoskeletal system and skin. The musculoskeletal system includes muscle, bone, articulated joints, cartilage, tendon, and ligament. Priority will be given to the establishment of collaborations between investigators with expertise in the zebrafish and investigators with expertise in the musculoskeletal systems and skin of mammals and humans.

NICHHD: Identification, cloning, and characterization of the genes important in normal development as well as those mutant genes that cause developmental defects. Elucidation of the cellular, biochemical, molecular, and genetic mechanisms underlying normal and defective development. This includes, but is not limited to, the study of general mechanisms of pattern formation and cell lineage, neural crest development, cell specification, differentiation, migration, and fate in early development of many organs/systems such as limb, nervous system, immune system, and heart.

NIDCD: Identification and cloning of genes/proteins involved in the normal and disordered development in the areas of hearing, balance, smell, taste, voice, speech, and language. Elucidation of the cellular, molecular, and biochemical mechanisms governing the proliferative, regenerative, lineage determination, and developmental capacities of these sensory cells and tissues.

NIDCR: All aspects of normal and abnormal craniofacial development, including genetics, complex origins of craniofacial disorders, cell lineages and differentiation, cell signaling and gene regulation, embryonic patterning, imaging, biomimetics, and new technologies for high-throughput genetic and protein screens.

NIDDK: Research on diabetes, particularly studies on pancreatic beta cell function and development, obesity and mechanisms underlying satiety, other endocrine and metabolic diseases, hematologic disorders, and diseases of the digestive system, liver, kidney, and urinary tract. Studies aiming to clarify the cellular and molecular events that dictate tissue and organ formation in all these systems are considered of relevance. These studies could include, but need not be limited to, studies to develop cell lines from any of the tissues or organs of interest, studies to characterize normal or abnormal function of tissues or organs of interest, methods to screen and identify additional mutations in these systems, and studies to define the molecular mechanisms that dictate cell-specific gene expression in relevant cell types.

NIDA: Identification of mechanisms underlying tolerance, sensitization, and addiction to drugs of abuse such as nicotine, amphetamine, cocaine, opiates, barbiturates, and hallucinogens. Identification of genetic suppressors and enhancers of the teratological effects of drugs of abuse on behavior and the nervous system. Processes involved in the development of brain regions and neurotransmitter systems mediating the hedonic and addictive properties of drugs of abuse.

NIEHS: Studies to examine the mechanism whereby environmental factors/agents alter any aspect of development. This includes the screening for mutants that ameliorate the toxicity of environmental agents, and the subsequent identification and characterization of the genes and pathways involved in their action. Characterization of the interactions among genetics, environmental agents, and time during development that lead to structural or functional abnormalities. Studies to examine the mechanistic pathways involved in developmental exposure to environmental agents and subsequent increased susceptibility to adult onset disease (developmental imprinting). Development of a mechanistically based model for testing environmental agents for developmental toxicity.

NIGMS: Development of novel methods for mutagenesis and manipulation of gene expression. Mutagenesis screens to identify and characterize genes that control fundamental biological mechanisms such as those that underlie gene regulation, chromosome organization and mechanics, cell growth and differentiation, pattern formation, sex determination, morphogenesis, cell cycle control, and behavior.

NIMH: Investigations that examine molecular, cellular, and biochemical bases of genetic mutations affecting neurogenesis, biological rhythms, learning, memory, and other cognitive functions and behaviors of the nervous system. These studies include, but are not limited to, development of screening methods for such mutations, identification, isolation, mapping, and functional analyses of the genes underlying mutations.

NINDS: Research on the development, normal function, and diseases of the nervous system. This research might include the use of mutants to understand the mechanisms controlling the following processes: neurogenesis, nervous system patterning, cell lineage, cell migration, programmed cell death, axon pathfinding and regeneration, myelination, and motor and sensory function. In addition, the utility of mutants as models for neurodegenerative diseases for use in translational research including therapeutic drug screens, functional neuroanatomy of the developing and adult nervous system, and use of optical imaging techniques to visualize neural activity is of particular interest.

The areas of interest listed above are not presented in any order of priority; they are only examples of areas of research to consider. Applications representing areas of interest to more than one Institute or Center will be assigned to multiple Institutes or Centers for funding consideration. Applicants are encouraged to propose work in other areas that are related to the objectives and scope of this PA.

MECHANISM OF SUPPORT

This PA will use the NIH individual research project grant (R01) award mechanism. Because the nature and scope of the research proposed in response to this PA may vary, it is anticipated that the size of awards will also vary. Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant.

Although this PA is the result of a trans-NIH initiative, awards will be made through the IC whose mission is most closely related to the proposed work. Through the TZCC, each funding component will share with the other committee members findings of any research supported as a result of this PA. All investigators funded under this initiative will be expected to work together cooperatively so that the information learned and the mutants and tools developed will be of maximum usefulness to the community.

This PA uses just-in-time concepts. It also uses the modular as well as the non-modular budgeting formats (see <http://grants.nih.gov/grants/funding/modular/modular.htm>). Specifically, if

you are submitting an application with direct costs in each year of \$250,000 or less, use the modular format. Otherwise follow the instructions for non-modular research grant applications.

ELIGIBLE INSTITUTIONS

You may submit (an) application(s) if your institution has any of the following characteristics:

- o For-profit or non-profit organizations
- o Public or private institutions, such as universities, colleges, hospitals, and laboratories
- o Units of State and local governments
- o Eligible agencies of the Federal government
- o Domestic or foreign

INDIVIDUALS ELIGIBLE TO BECOME PRINCIPAL INVESTIGATORS

Any individual with the skills, knowledge, and resources necessary to carry out the proposed research is invited to work with their institution to develop an application for support. Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are always encouraged to apply for NIH programs.

SPECIAL REQUIREMENTS

Restricted availability of unique research resources, upon which further studies are dependent, can impede the advancement of research. Conversely, sharing biomaterials, reagents, data, and software in a timely manner has been an essential element in the rapid progress that has been made in research on zebrafish and other non-mammalian model organisms. NIH policy requires that investigators make unique research resources readily available for research purposes to qualified individuals within the scientific community after publication [NIH Grants Policy Statement (http://grants.nih.gov/grants/policy/nihgps_2001/index.htm); Principles and Guidelines for Recipients of NIH Research Grants and Contracts on Obtaining and Disseminating Biomedical Research Resources: Final Notice, December 1999 (http://ott.od.nih.gov/NewPages/RTguide_final.html)].

The NIH is interested in ensuring that the research resources (constructs, reagents, cell lines, software tools, expression data, methods, etc.) developed through this PA become readily available to the research community for further research, development, and application, in the expectation that this will lead to products and knowledge of benefit to the public. At the same

time, NIH recognizes the rights of grantees to elect and retain title to subject inventions developed under federal funding under the provision of the Bayh-Dole Act.

This PA has two special requirements regarding research resources produced in proposed projects:

(1) Applicants are required to include in their applications a specific plan by which they will share research resources with the wider scientific community, including but not limited to: mutant fish, embryos, and sperm, genetic and phenotypic screens, mutagenesis protocols, and genetic and phenotypic data for all mutant strains. The National Resource for Zebrafish at the University of Oregon (http://zfin.org/zf_info/stckctr/stckctr.html), with its associated Zebrafish Information Network database (ZFIN; http://zfin.org/cgi-bin/webdriver?Mlval=aa-ZDB_home.apg), is the focal point for sharing of resources among investigators using zebrafish. Plans to share materials generated by projects under this PA through the National Resource for Zebrafish should include evidence/documentation of coordination with investigators at the Resource. A reasonable time frame for periodic deposition of mutants, sperm, reagents, and data should be specified in the application and will be considered during the review of the plan for sharing.

(2) Applicants are required to include a plan addressing if, or how, they will exercise their intellectual property rights while making available to the broader scientific community patentable research resources. The plan should address the following questions:

- o Will material transfers be made with no more restrictive terms than in the Simple Letter MTA or the UBMTA?
- o Will there be reach-through requirements on materials transferred?
- o Should any intellectual property arise that requires a patent, will the technology remain widely available to the research community?

Both the sharing and intellectual property plans should, at a minimum, address these elements in a clear and concise manner. Applicants are encouraged to inform and/or confer with their institutional offices of technology transfer to develop plans for addressing these requirements.

Applicants are reminded that the grantee institution is required to disclose each subject invention to NIH within two months after the inventor discloses it in writing to grantee institutional personnel responsible for patent matters. The awarding Institute reserves the right to monitor awardee

activity in this area to ascertain if patents or patent applications on zebrafish identified through phenotypic screens, and phenotypic and genotypic data for all zebrafish strains or other patentable subject matter are adversely affecting the goals of this PA.

WHERE TO SEND INQUIRIES

We encourage your inquiries concerning this PA and welcome the opportunity to answer questions from potential applicants. For general inquiries contact:

Dr. Lorette Javois
Center for Research for Mothers and Children
National Institute of Child Health and Human Development
6100 Executive Boulevard, Room 4B01, MSC 7510
Bethesda, MD 20892-7510
Telephone: (301) 496-5541
FAX: (301) 480-0303
Email: lj89j@nih.gov

Inquiries may fall into three areas: scientific/research, peer review, and financial or grants management issues. A complete listing of contacts for programmatic, review, and fiscal/administrative inquiries may be found at:

http://www.nichd.nih.gov/PA/Zebrafish_GeneticStudies.htm.

LETTER OF INTENT

Prospective applicants are asked to submit a letter of intent that includes the following information:

- o Descriptive title of the proposed research
- o Name, address, and telephone number of the Principal Investigator
- o Names of other key personnel
- o Participating institutions
- o Number and title of this PA

Although a letter of intent is not required, is not binding, and does not enter into the review of a subsequent application, the information that it contains allows NIH staff to estimate the potential review workload and plan the review.

The letter of intent is to be sent by the date listed at the beginning of this document. The letter of intent should be sent to:

Dr. Lorette Javois
Center for Research for Mothers and Children
National Institute of Child Health and Human Development
6100 Executive Boulevard, Room 4B01, MSC 7510
Bethesda, MD 20892-7510
Telephone: (301) 496-5541
FAX: (301) 480-0303
Email: lj89j@nih.gov

SUBMITTING AN APPLICATION

Applications must be prepared using the PHS 398 research grant application instructions and forms (rev. 5/2001). The PHS 398 is available at <http://grants.nih.gov/grants/funding/phs398/phs398.html> in an interactive format. For further assistance contact GrantsInfo, Telephone (301) 435-0714, Email: GrantsInfo@nih.gov.

APPLICATION RECEIPT DATES: Applications submitted in response to this program announcement will be accepted on November 19, 2002, 2003, and 2004.

SPECIFIC INSTRUCTIONS FOR MODULAR GRANT APPLICATIONS: Applications requesting up to \$250,000 per year in direct costs must be submitted in a modular grant format. The modular grant format simplifies the preparation of the budget in these applications by limiting the level of budgetary detail. Applicants request direct costs in \$25,000 modules. Section C of the research grant application instructions for the PHS 398 (rev. 5/2001) at <http://grants.nih.gov/grants/funding/phs398/phs398.html> includes step-by-step guidance for preparing modular grants. Additional information on modular grants is available at <http://grants.nih.gov/grants/funding/modular/modular.htm>.

SPECIFIC INSTRUCTIONS FOR APPLICATIONS REQUESTING MORE THAN \$250,000 BUT LESS

THAN \$500,000: Applicants planning on requesting more than \$250,000 but less than \$500,000 in direct costs for any year are urged to contact program staff at the IC whose mission is most closely related to the proposed work before submitting the application to discuss the budget.

SPECIFIC INSTRUCTIONS FOR APPLICATIONS REQUESTING \$500,000 OR MORE PER YEAR:

Applications requesting \$500,000 or more in direct costs for any year must include a cover letter identifying the NIH staff member within one of NIH institutes or centers who has agreed to accept assignment of the application.

Applicants requesting more than \$500,000 must carry out the following steps:

- 1) Contact the IC program staff at least six weeks before submitting the application, i.e., as you are developing plans for the study;
- 2) Obtain agreement from the IC staff that the IC will accept your application for consideration for award; and,
- 3) Identify, in a cover letter sent with the application, the staff member and IC who agreed to accept assignment of the application.

This policy applies to all investigator-initiated new (type 1), competing continuation (type 2), or any amended or revised version of these application types. Additional information on this policy is available in the NIH Guide for Grants and Contracts, October 19, 2001 at <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-004.html>.

ADDITIONAL INSTRUCTIONS: Please describe your plans to share research resources and to exercise your intellectual property rights in a brief section immediately following the Research Plan (see SPECIAL REQUIREMENTS). The section addressing these plans is limited to three pages in length.

SENDING AN APPLICATION TO THE NIH: Submit a signed, typewritten original of the application, including the checklist, and five signed photocopies in one package to:

Center for Scientific Review
National Institutes of Health
6701 Rockledge Drive, Room 1040, MSC 7710
Bethesda, MD 20892-7710
Bethesda, MD 20817 (for express/courier service)

APPLICATION PROCESSING: Applications must be received by or mailed on or before the receipt dates listed above. The CSR will not accept any application in response to this PA that is essentially the same as one currently pending initial review unless the applicant withdraws the pending application. The CSR will not accept any application that is essentially the same as one already reviewed. This does not preclude the submission of a substantial revision of an application already reviewed, but such application must include an Introduction addressing the previous critique.

PEER REVIEW PROCESS

Applications submitted for this PA will be assigned on the basis of established PHS referral guidelines. A special emphasis panel convened in accordance with the standard NIH peer review procedures (<http://www.csr.nih.gov/refrev.htm>) will evaluate applications for scientific and technical merit.

As part of the initial merit review, all applications will:

- o Receive a written critique
- o Undergo a selection process in which only those applications deemed to have the highest scientific merit, generally the top half of applications under review, will be discussed and assigned a priority score
- o Receive a second level review by the appropriate national advisory council or board

REVIEW CRITERIA

The goals of NIH-supported research are to advance our understanding of biological systems, improve the control of disease, and enhance health. In the written comments, reviewers will be asked to discuss the following aspects of your application in order to judge the likelihood that the proposed research will have a substantial impact on the pursuit of these goals:

- o Significance
- o Approach
- o Innovation
- o Investigator
- o Environment

The scientific review group will address and consider each of these criteria in assigning your application's overall score, weighting them as appropriate for each application. Your application does not need to be strong in all categories to be judged likely to have major scientific impact and thus deserve a high priority score. For example, you may propose to carry out important work that by its nature is not innovative but is essential to move a field forward.

(1) SIGNIFICANCE: Does your study address an important problem? If the aims of your application are achieved, how do they advance scientific knowledge? What will be the effect of these studies on the concepts or methods that drive this field?

(2) APPROACH: Are the conceptual framework, design, methods, and analyses adequately developed, well integrated, and appropriate to the aims of the project? Do you acknowledge potential problem areas and consider alternative tactics?

(3) INNOVATION: Does your project employ novel concepts, approaches or methods? Are the aims original and innovative? Does your project challenge existing paradigms or develop new methodologies or technologies?

(4) INVESTIGATOR: Are you appropriately trained and well suited to carry out this work? Is the work proposed appropriate to your experience level as the principal investigator and to that of other researchers (if any)?

(5) ENVIRONMENT: Does the scientific environment in which your work will be done contribute to the probability of success? Do the proposed experiments take advantage of unique features of the scientific environment or employ useful collaborative arrangements? Is there evidence of institutional support?

ADDITIONAL REVIEW CRITERIA: In addition to the above criteria, your application will also be reviewed with respect to the following:

PROTECTIONS: The adequacy of the proposed protection for humans, animals, or the environment, to the extent they may be adversely affected by the project proposed in the application.

DATA SHARING: The scientific review group will evaluate the adequacy of the proposed plans for sharing and data access. Comments on the plan and any concerns will be presented in an administrative note in the Summary Statement.

BUDGET: The reasonableness of the proposed budget and the requested period of support in relation to the proposed research.

AWARD CRITERIA

Applications submitted in response to a PA will compete for available funds with all other recommended applications. The following will be considered in making funding decisions:

- o Scientific and technical merit of the proposed project as determined by peer review;
- o Cost effectiveness of the proposed strategy;
- o Adequacy of plans to make widely available to the research community in a timely manner all research resources developed during the project; the sharing plan as approved, after negotiation with the applicant when necessary, will be a condition of the award; evaluation of non-competing continuation applications will include assessment of the effectiveness of research resource release;
- o Adequacy of plans to exercise (or not exercise) intellectual property rights while permitting wide availability to the research community of patentable research resources developed during the project;
- o Program priorities and program balance;
- o Availability of funds.

REQUIRED FEDERAL CITATIONS

PUBLIC ACCESS TO RESEARCH DATA THROUGH THE FREEDOM OF INFORMATION ACT: The Office of Management and Budget (OMB) Circular A-110 has been revised to provide public access to research data through the Freedom of Information Act (FOIA) under some circumstances. Data that are (1) first produced in a project that is supported in whole or in part with Federal funds and (2) cited publicly and officially by a Federal agency in support of an action that has the force and effect of law (i.e., a regulation) may be accessed through FOIA. It is important for applicants to understand the basic scope of this amendment. NIH has provided guidance at http://grants.nih.gov/grants/policy/a110/a110_guidance_dec1999.htm

URLs IN NIH GRANT APPLICATIONS OR APPENDICES: All applications and proposals for NIH funding must be self-contained within specified page limitations. Unless otherwise specified in an NIH solicitation, Internet addresses (URLs) should not be used to provide information necessary to the review because reviewers are under no obligation to view the Internet sites. Furthermore, we caution reviewers that their anonymity may be compromised when they directly access an Internet site.

HEALTHY PEOPLE 2010: The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2010," a PHS-led national activity for setting priority areas. This PA is related to one or more of the priority areas. Potential applicants may obtain a copy of "Healthy People 2010" at <http://www.health.gov/healthypeople>.

AUTHORITY AND REGULATIONS: This program is described in the Catalog of Federal Domestic Assistance Nos. 93.865, 93.396, 93.306, 93.867, 93.837, 93.839, 93.172, 93.866, 93.273, 93.846, 93.173, 93.121, 93.849, 93.279, 93.113, 93.862, 93.242, 93.853 and is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review. Awards are made under authorization of Sections 301 and 405 of the Public Health Service Act as amended (42 USC 241 and 284) and administered under NIH grants policies described at <http://grants.nih.gov/grants/policy/policy.htm> and under Federal Regulations 42 CFR 52 and 45 CFR Parts 74 and 92.

The PHS strongly encourages all grant recipients to provide a smoke-free workplace and discourage the use of all tobacco products. In addition, Public Law 103-227, the Pro-Children Act of 1994, prohibits smoking in certain facilities (or in some cases, any portion of a facility) in which regular or routine education, library, day care, health care, or early childhood development services are provided to children. This is consistent with the PHS mission to protect and advance the physical and mental health of the American people.

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